The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 24

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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Ex parte NOBUTO YAMAMOTO

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Appeal No. 1999-1389
Application No. 08/618,485

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ON BRIEF

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Before WILLIAM F. SMITH, ADAMS, and MILLS Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-4, which are all the claims pending in the application.

Claims 1 and 2 are illustrative of the subject matter on appeal and are reproduced below:

1. A process for cloning vitamin D_3-binding protein (Gc protein) into baculovirus comprising the step of selecting and using a baculovirus vector to clone the vitamin D_3-binding protein (Gc protein).

2. A process for producing a cloned macrophage activating factor (GcMAFc) comprising contacting cloned vitamin D_3 binding protein in vitro with immobilized ß-galactosidase and sialidase and obtaining the cloned macrophage activating factor (GcMAFc).

Claims 3 and 4 differ from claims 1 and 2 only in that claim 3 is a process for cloning vitamin D_3-binding protein domain III, and claim 4 is a process for producing cloned macrophage activating factor CdMAF wherein cloned vitamin D_3-binding protein domain III is contacted with ß-galactosidase and sialidase.

The references relied upon by the examiner are:

Yamamoto 5,177,002 Jan. 5, 1993

Cooke et al. (Cooke), "Serum Vitamin D-binding Protein is a Third Member of the Albumin and α Fetoprotein Gene Family," J. Clin. Invest., Vol. 76, pp. 2420-2424 (1985)

Luckow, Protein Production and Processing from Baculovirus Expression Vectors, in Insect Cell Cultures: Biopesticide and Protein Production Shuler et al. eds., John Wiley and Sons pp. 1-38 (1993)

GROUND OF REJECTION

Claim 1-4 stand rejected under 35 U.S.C. § 103 as being unpatentable over Yamamoto in view of Luckow and Cooke.

We affirm the rejection under 35 U.S.C. § 103 of claims 1 and 2, and reverse the rejection of claims 3 and 4.

DISCUSSION

In reaching our decision in this appeal, we have given careful consideration to the appellant's specification and claims, and to the respective positions articulated by the appellant and the examiner. We make reference to the examiner's Answer[1] for the examiner's reasoning in support of the rejection. We further reference appellant's Brief[2], and appellant's Reply Brief[3] for the appellant's arguments in favor of patentability.

CLAIM GROUPING:

Appellant presents (Brief, page 3) two claim groupings. Group I (claims 1 and 2) do not stand or fall together with Group II (claims 3 and 4).

THE REJECTIONS UNDER 35 U.S.C. § 103:

Initially, appellant argues (Brief, pages 3-4) that the examiner cited the wrong Yamamoto reference in his statement of the rejection. Appellant argues (Brief, page 4) that "the rejection must be withdrawn (and properly restated in another Office Action, if desired), as it does not show how the cited references combine to make a prima facie case of obviousness." Appellant's arguments have been considered and are not persuasive. Appellant not only had notice of the correct Yamamoto reference (Brief, page 5, "the intended combination of references including Yamamoto (BB)…."), but responded to the examiner's position (Brief, pages 4-10) with reference to the correct Yamamoto reference.

[1] Paper No. 21, mailed September 1, 1998.
[2] Paper No. 20, received June 24, 1998.
[3] Paper No. 22, received October 30, 1998.

In our opinion, given that appellant had notice of the typographical error in the Yamamoto reference designation and responded to the examiner's rejection in view of the correct Yamamoto reference, we find that the typographical error on behalf of the examiner did not prejudice appellant's case. According we find the do not Final Rejection fatally flawed by the examiner's typographical error. Therefore, we move forward to the merits of the examiner's rejection.

According to the examiner (Answer, page 3) Yamamoto disclose "a process of converting glycosylated Gc protein obtained from pooled blood to a highly potent macrophage activating factor (GcMAF) by contacting Gc protein with immobilized ß-galactosidase and sialidase." The examiner explains (Answer, page 4) that Yamamoto discloses "that Gc protein is also known as vitamin D-binding protein and that the nucleotide and amino acid sequences of Gc protein [including domain III] was reported by Cooke." The examiner relies on Luckow (Answer, page 4) to teach "a process for the abundant expression of exogenous proteins in insect cells using baculovirus expression vectors."

The examiner concludes (pages 5-6) that:

> One of ordinary skill in the art would be motivated to combine these teachings because cloning Gc protein in a baculovirus vector facilitates the abundant and economical expression of a glycosylated Gc protein that is antigenically, immunogenically, and functionally similar to its counter part isolated from natural sources on a scale that is not technically or economically feasible with other expression systems, and because the cloned Gc protein could be converted to GcMAF, a highly potent macrophage activating factor, which has utility as a therapeutic agent for inducing macrophage activation, as taught by Yamamoto et al. …
>
> Furthermore, it would have been obvious to one of ordinary skill in the art at the time of Appellant's invention to clone the cDNA encoding domain III of the Gc protein, as taught by Cooke et al., into a

> baculovirus vector, as taught by Luckow, and to express the cloned domain III of the Gc protein in insect cells, as taught by Luckow, as recited in claim 3, with a reasonable expectation of success. Furthermore, it would have been obvious to one of ordinary skill in the art at the time of Appellant's invention to contact the recombinantly expressed domain III of the Gc protein in vitro with immobilized ß-galactosidase and sialidase, as taught by Yamamoto, as recited in claim 4, with a reasonable expectation of success.

Claims 1 and 2:

Appellant argues (Brief, page 6) that "the Office fails to show how or where Luckow teaches that baculovirus could be successfully employed to express vitamin D binding protein (i.e., Gc protein) in insects." Appellant argues (Brief, page 7) that Luckow "acknowledges the unpredictability of foreign protein expression by baculovirus vectors" because Luckow recognize "differences in the microheterogeneity of oligosaccharide structures are often observed for mammalian glycoproteins expressed in different mammalian cell lines or by individual cell lines under different culture conditions." In response to appellant's arguments the examiner argues (Answer, page 7) that "Luckow teaches at the paragraph bridging pages 15-16 that many baculovirus-expressed glycoproteins retain full biologic activity in in vitro assays, which would create a reasonable expectation of successfully using baculovirus vectors and insect cells for the abundant and economical expression of a glycosylated Gc protein."

With reference to Ausubel[4], appellant argues (Brief, page 8) that "one skilled in the art would not have had any such expectation of abundant, economical and

[4] Expression of Protein in Insect Cells Using Baculoviral Vectors, in Current Protocols in Molecular Biology, 6.8.1-6.11.7 (Ausubel et al., eds., Greene Publishing and Wiley-Interscience, New York 1990).

effective expression of Gc protein because 'the ability of a given recombinant virus to produce large quantities of foreign proteins must be determined empirically.'" We note however, that appellant's three quotations from Ausubel span 25 pages. Within those 25 pages, Ausubel also discusses the popularity of the baculovirus system, in addition to a number of advantages in using the system, e.g., "[o]ne of the beauties of this expression system is a visual screen allowing recombinant viruses to be distinguished [16.8.3]."

The initial burden of presenting a prima facie case of obviousness rests on the examiner. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). In meeting this initial burden of establishing a prima facie case of obviousness, there must be both some suggestion or motivation to modify the references or combine reference teachings and a reasonable expectation of success. In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). As set forth in In re O'Farrell, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 "[o]bviousness does not require absolute predictability of success … [f]or obviousness under § 103, all that is required is a reasonable expectation of success" [citations omitted].

In our judgment, on these facts, we find that the examiner met his burden of establishing that a person of ordinary skill in the art would have had a reasonable expectation of success in cloning vitamin D_3-binding protein into baculovirus comprising the step of selecting and using a baculovirus vector, and in producing macrophage activating factor comprising using the cloned vitamin D_3 binding protein in the method disclosed by Yamamoto.

Accordingly, we affirm the rejection of claims 1 and 2 under 35 U.S.C. § 103 as being unpatentable over Yamamoto in view of Luckow and Cooke.

Claims 3 and 4:

Appellant argues (Brief, page 9) that "[a]lone or in combination, none of the applied references disclose that domain III is responsible for the macrophage activating function of the protein, or that domain III could be independently cloned while preserving its structural and functional integrity."

In response, the examiner emphasizes, inter alia, that Cooke teach domain III of the vitamin D_3 binding protein. However, to establish a prima facie case of obviousness, there must be both some suggestion or motivation to modify the references or combine reference teachings and a reasonable expectation of success. In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). On this record, the examiner fails to identify a suggestion in the prior art to specifically clone domain III of the vitamin D_3-binding protein. The examiner also fails to identify a suggestion to combine domain III of vitamin D_3 binding protein with immobilized ß-galactosidase and sialidase to obtain macrophage activating factor. Furthermore, the examiner fails to explain how the applied combination of references would provide one with a reasonable expectation of success that the combination of domain III of vitamin D_3 with ß-galactosidase and sialidase would result in obtaining macrophage activating factor.

Accordingly, we reverse the rejection of claim 3 and 4 under 35 U.S.C. § 103 as being unpatentable over Yamamoto in view of Luckow and Cooke.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED - IN - PART

William F. Smith Administrative Patent Judge	))))) BOARD OF PATENT
Donald E. Adams Administrative Patent Judge	)) APPEALS AND)) INTERFERENCES
Demetra J. Mills Administrative Patent Judge	))

DA/dm

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